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10/530,035	08/29/2005	Bent Karsten Jakobsen	006090.00018	2934

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,035	JAKOBSEN ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-37* is/are pending in the application.

4a) Of the above claim(s) *16,19-22,24,25 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-15,17,18,23,26 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 2/12/08, is acknowledged.

Claims 1 and 15-16 have been amended.
Claims 2-4 have been cancelled.
Claims 1 and 5-37 are pending.

2. Applicant's election of group I, claims 1, 5-18 and 23-32, in the reply filed on 2/12/08 is acknowledged. Applicant has further elected SEQ ID NO: 1 as the species of linker, and a monovalent HLA-A2 Tax specific TCR comprising a variable and constant domain from the same species, as the species of scTCR.

Claims 19-22 and 33-37 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 16, 24-25, and 27-29 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species.

Claims 1, 5-15, 17-18, 23, 26, and 30-32 read on the elected invention and are being acted upon.

3. The information disclosure statement, filed on 4/1/05, is acknowledged. However, Chung et al. has been lined through since a copy of the reference could not be located in the file.

4. Claim 5 is objected to for being dependent from cancelled claim 3.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-15, 17-18, 23, 26, and 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1 and 18 are indefinite in the recitation of TRAC*01, TRBC1*01, TRBC2*01, etc. The instant specification does not define "TRAC*01", but it appears to be a designation for allele 1 of the human T cell receptor alpha chain constant region. The specification on page 10 provides sequences

corresponding to the residues intended for cysteine substitution. However, said sequences comprise human TCR constant region sequences. The instant claims are clearly not limited to human scTCRs, as evidenced by dependent claim 25, which recites that the constant region sequences are those of a mouse TCR. The fact that the claims are not limited to human TCRs renders the claims indefinite. For example, the specification on page 10 teaches the sequence of the murine TCR alpha constant domain (i.e. murine TRAC). However, amino acid 48 of murine TRAC is not Thr, as recited in the claims, but comprises a Lys residue (in contrast, residue 49 of mouse TRAC is Thr). It is unclear how the claims can encompass a soluble mouse TCR in which Thr 48 of TRAC has been substituted, when in fact amino acid 48 of mouse TRAC is Lys.

B) Claims 1 and 18 are indefinite since they comprise numerous grammatical errors. For example, claims 1 and 18 recite that the segment includes a sequence "corresponding corresponds" to TRAC. Additionally, the claims contain spacing errors, for example line 18 of claim 1 recites "ofTCRBC1".

C) Claims 1 and 18 recite the limitation "said non-native disulfide bond" in lines 16 and 4, respectively. There is insufficient antecedent basis for this limitation in the claim.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 5-14, 17-18, 23, 26, and 30-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 and 20 of U.S. Patent No. 7,329,731 in view of WO 99/18129 (of record), and WO 99/60120.

The '731 patent claims a soluble TCR (sTCR) comprising a TCR α and β variable region and a constant region extracellular sequence including a sequence of TRAC*01 and TRBC1*01 or TRBC2*02, wherein a disulfide bond links cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01. The '731 patent further claims mutating or truncating the TCR constant region to remove the native disulfide bond. The '731 patent further claims a pharmaceutical formulation comprising the sTCR and a sTCR associated with a therapeutic agent or label (i.e. a particle). Furthermore, it would have been obvious to further include a linker sequence linking the C terminus of the α segment to the N terminus of the β segment, since WO 99/18129 teaches the usefulness of peptide linkers in effectively positioning the Vα and Vβ chains (see pages 14-16 and 23-25, in particular). Additionally, it would have been obvious to make a sTCR, as claimed in the '731 patent, specific to HLA-A2 tax, since WO 99/60120 teaches the usefulness of HLA-A2 tax specific sTCRs for therapeutic and diagnostic purposes (see pages 21-22 and 52 in particular).

8. Claim 1, 5-14, 17-18, 23, 26, and 30-32 are **provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 9-20 of copending Application No. 11/667,276 in view of** WO 99/18129 (of record), and WO 99/60120.

The '276 application claims a soluble TCR (sTCR) comprising a TCR α and β variable region and a constant region extracellular sequence including a sequence of TRAC*01 and TRBC1*01 or TRBC2*02, wherein a disulfide bond linking cysteine residues

substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01. The '276 application further claims mutating or truncating the TCR constant region to remove the native disulfide bond. The '276 application further claims a sTCR associated with a superantigen (i.e. a therapeutic agent) or label. Furthermore, it would have been obvious to further include a linker sequence linking the C-terminus of the α segment to the N terminus of the β segment, since WO 99/18129 teaches the usefulness of peptide linkers in effectively positioning the Vα and Vβ chains (see pages 14-16 and 23-25, in particular). Additionally, it would have been obvious to make a sTCR, as claimed in the '276 application, specific to HLA-A2 tax, since WO 99/60120 teaches the usefulness of HLA-A2 tax specific sTCRs for therapeutic and diagnostic purposes (see pages 21-22 and 52 in particular).

This is a provisional obviousness-type double patenting rejection.

9. Claim 1, 5-15, 17-18, 23, 26, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 10-19, and 31 of copending Application No. 11/664,214 in view of WO 99/60120.

The '214 application claims a soluble single chain TCR (scTCR) comprising a TCR α and β variable region and a constant region extracellular sequence including a sequence of TRAC*01 and TRBC1*01 or TRBC2*02, wherein a disulfide bond linking cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01. The '214 application further claims mutating or truncating the TCR constant region to remove the native disulfide bond. The '214 application further claims a pharmaceutical composition comprising the scTCR, and a scTCR associated with a therapeutic agent. Furthermore, the '214 application claims a scTCR joined by a linker peptide comprising SEQ ID NO: 1, wherein the peptide links the C-terminus of the α segment to the N terminus of the β segment. Additionally, it would have been obvious to make a sTCR, as claimed in the '214 application, specific to HLA-A2 tax, since WO 99/60120 teaches the usefulness of HLA-A2 tax specific sTCRs for therapeutic and diagnostic purposes (see pages 21-22 and 52 in particular).

This is a provisional obviousness-type double patenting rejection.

10. Claim 1, 5-14, 17-18, 23, 26, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 86, and 88-89 of copending Application No. 10/532,879 in view of WO 99/18129 (of record), and WO 99/60120.

The '879 application claims a soluble single chain TCR (scTCR) comprising a TCR α and β variable region and a constant region extracellular sequence including a sequence of TRAC*01 and TRBC1*01 or TRBC2*02, wherein a disulfide bond linking cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01. Furthermore, it would have been obvious to further include a linker sequence linking the C-terminus of the α segment to the N terminus of the β segment, since WO 99/18129 teaches the usefulness of peptide linkers in effectively positioning the Vα and Vβ chains (see pages 14-16 and 23-25, in particular). Additionally, it would have been obvious to make a sTCR, as claimed in the '879 application, specific to HLA-A2 tax, since WO 99/60120 teaches the usefulness of HLA-A2 tax specific sTCRs for therapeutic and diagnostic purposes (see pages 21-22 and 52 in particular).

This is a provisional obviousness-type double patenting rejection.

11. Claim 1, 5-15, 17-18, 23, 26, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23, 26-35, 40-43, 5and 4-55 of copending Application No. 10/535,965 in view of WO 99/60120.

The '965 application claims a soluble single chain TCR (scTCR) comprising a TCR α and β variable region and a constant region extracellular sequence including a sequence of TRAC*01 and TRBC1*01 or TRBC2*02, wherein a disulfide bond linking cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01. The '965 application further claims mutating or truncating the TCR constant region to remove the native disulfide bond. The '965 application further claims a pharmaceutical composition comprising the scTCR, and a scTCR associated with a therapeutic agent. Furthermore, the '965 application claims a scTCR joined by a linker peptide comprising SEQ ID NO: 1, wherein the peptide links the C-terminus of the α segment to the N terminus of the β segment. Additionally, it would have been obvious to make a

scTCR, as claimed in the '965 application, specific to HLA-A2 tax, since WO 99/60120 teaches the usefulness of HLA-A2 tax specific sTCRs for therapeutic and diagnostic purposes (see pages 21-22 and 52 in particular).

This is a provisional obviousness-type double patenting rejection.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes, Ph.D.

Patent Examiner

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/G.R. Ewoldt/

Primary Examiner, Art Unit 1644